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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,674	06/12/2006	Herve Perron	128125	7417

25944 7590 09/11/2008

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EXAMINER	
KOLKER, DANIEL E	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
09/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,674	PERRON ET AL.	
	Examiner	Art Unit	
	DANIEL KOLKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *1 and 11-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7 and 10* is/are rejected.

7)☒ Claim(s) *8 and 9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/1/06,9/8/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks filed 2 July 2008 have been entered. Claims 1 – 15 are pending.

Election/Restrictions

2. Applicant's election with traverse of Group 2 (claims 2 – 10) in the reply filed on 2 July 2008 is acknowledged. The traversal is on the ground(s) that the examiner has failed to provide evidence that lack of unity exists, as the examiner has not provided evidence that both heterocomplex GM2AP/GM2/MRP14 and mutated GM2AP/GM2/MRP14 were known in the prior art. This is not found persuasive because the first claimed technical feature is not both of these complexes, but rather either of these complexes. Note claim 1 lists the two complexes in the alternative. Applicant is directed to MPEP § 1850(II), which states that in those cases where an invention is claimed as elements A+X, and another invention is claimed as elements A+Y, a showing that A alone was known in the prior art is sufficient to establish lack of unity. That situation is analogous to the present situation. As the examiner properly found that the heterocomplex GM2AP/GM2/MRP14 was known (see Roecklin WO 01/05422; cited in previous office action), the first claimed product is not a contribution over the prior art and therefore is not a special technical feature as defined by PCT Rule 13.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1 and 11 – 15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2 July 2008.

4. Claims 2 – 10 are under examination.

Information Disclosure Statement

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892 or by applicant in one of the IDSs of record, they have not been considered.

Priority

6. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2 – 3 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Roecklin (WO 01/05422, of record) as evidenced by U.S. Patent 7,081,345 (cited on IDS filed 1 September 2006). The ‘345 patent is the national-stage entry of the international application that formed the basis of the Roecklin ‘422 publication and as such the ‘345 patent is a translation of the ‘422 publication. Reference to specific passages of text are to the ‘345 patent unless otherwise indicated.

Roecklin teaches isolating a cytotoxic factor from urine of patients with multiple sclerosis (MS). Beginning at column 46 line 55 and continuing through column 48 line 22, the patent explains in detail how to purify the cytotoxic factor. While the reference does not explicitly identify the factor as being a heterocomplex of GM2AP/GM2/MRP14 as recited in instant claim 2, the starting materials and procedures detailed in the ‘345 patent (and therefore also in the '422 publication) are the same as those that appear as Example 2 of the present specification. Since Example 2 is indicated to be a suitable method to isolate the cytotoxic complex from urine, and the sole step of instant claim 2 is isolation of the complex from a biological sample, these same steps which are taught in the prior art reference anticipate claim 2.

Claim 3 is anticipated as Roecklin also teaches that the cytotoxic factor can be detected in an ELISA assay. See Example 14 spanning columns 54 – 55. Note urine samples are used (column 55 line 4) and are captured with anti-GM2AP antibody. This antibody will bind to the heterocomplex, as GM2AP is one of the components of the heterocomplex. The amount of polyclonal antibody bound to the heterocomplex is detected with anti-rabbit IgG antibodies (column 55 first complete paragraph). Claim 10 is anticipated as urine is used as the biological sample in this example.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2 – 5 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roecklin (WO 01/05422, of record) as evidenced by U.S. Patent 7,081,345 (cited on IDS filed 1 September 2006) and in view of Hornbeck 2000 (Current Protocols in Molecular Biology 11.2.1 – 11.2.22).

The reasons why claims 2 – 3 and 10 are anticipated by Roecklin are set forth in the rejection under 35 USC 102(b) above. Roecklin teaches that GM2AP protein is present in urine samples from patients with multiple sclerosis, and teaches ELISA assays to detect GM2AP, wherein a single antibody against GM2AP is used. However Roecklin does not teach such detection assays wherein two antibodies against the same protein are used, as encompassed by claims 4 – 5.

Hornbeck teaches several types of ELISA protocols, including the antibody-sandwich assay, which uses two antibodies, one being a capture antibody and the other being a detection antibody. See for example pages 11.2.8 – 11.2.10. This is on point to claims 4 – 5; note that neither of these claims requires that the antibodies bind to different proteins within the complex. The claims are sufficiently broad that they read on using two antibodies against the same protein in an ELISA. Hornbeck teaches that the antibody sandwich form of ELISA is particularly suited to detecting soluble antigens, and it is 2 – 5 times more sensitive than those in which the

antigen is bound to the solid phase. However Hornbeck does not teach assays for detecting the heterocomplex of GM2AP/GM2/MRP14 as recited in claim 2.

It would have been obvious to one of ordinary skill in the art to modify the methods taught by Roecklin to use an antibody sandwich ELISA as taught by Hornbeck, thereby arriving at the invention of claims 4 – 5. The motivation to do so would be to use a more sensitive assay, as Hornbeck teaches that the double antibody sandwich assay is particularly sensitive and is suited to detecting soluble antigens, such as those that Roecklin teaches are present in the urine of patients with multiple sclerosis.

9. Claims 2 – 7 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roecklin in view of Hornbeck as applied to claims 2 – 5 and 10 above, and further in view of Perron 2004 (6th International Symposium on Neuroviroloogy and the HIV Neuroprotection Workshop, September 10 – 14, 2004, published in Journal of Neurovirology 10 (Suppl. 3):p. 124).

The reasons why claims 2 – 5 and 10 are obvious over Roecklin in view of Hornbeck are set forth above. While Roecklin teaches ELISAs for detection of GM2AP, and Hornbeck teaches methods of using multiple antibodies in ELISAs including use of capture and detection antibodies, which is on point to claim 7, neither reference teaches using one antibody that binds to MG2AP and another antibody that binds to MRP14 as recited in claim 6.

Perron teaches that the cytotoxic factor specifically found in the urine of patients with multiple sclerosis is a heterocomplex comprised of GM2AP, S100A9 (which is synonymous with MRP14; see for example Roecklin '345 patent page 2, third cited reference (by Rafferty et al.), which identifies the two terms as synonymous), and GM2. This is on point to claim 2, drawn to a method of detecting a heterocomplex comprising GM2AP, GM2, and MRP14, as well as claim 6, which is on point to detecting two separate proteins within the complex. However Perron does not teach methods of detection using at least two antibodies as recited in claim 6.

It would have been obvious to one of ordinary skill in the art to use an antibody against GM2AP, taught by Roecklin, and an antibody against MRP14 (also known as S100A9), as suggested by Perron, thereby arriving at the method of claim 6. The motivation to do so would be to detect the level of the cytotoxic complex, as Perron teaches that the complex itself is cytotoxic and diagnostic of multiple sclerosis. Additionally, it would have been obvious to one of

ordinary skill in the art to use a capture antibody and detection antibody, as suggested by Hornbeck, as these are parts of the assays taught by Hornbeck to be of high sensitivity.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2 – 5 and 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 76 – 77 of copending Application No. 11/450360. Although the conflicting claims are not identical, they are not patentably distinct from each other because in each case the claims encompass detection of a heterocomplex comprising calgranulin B. Note that claims 76 – 77 of the '360 application use

this name, but the instant specification indicates that this is a synonym for MRP14 (p. 4). Thus in each application the claims encompass detection of the same protein. Note that instant claims 2 - 5 do not require detection of multiple proteins of the heterocomplex; the methods are sufficiently broad that they encompass detecting one molecule of the complex when it is part of such a complex.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Claims 2 – 5 and 10 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8 – 9 of U.S. Patent No. 7,081,345. Although the conflicting claims are not identical, they are not patentably distinct from each other because in each case the claims encompass detection of a heterocomplex comprising GM2AP. Note that SEQ ID NO:9 in the '345 patent is identified as being GM2AP (see '345 patent column 5 lines 15 – 25). In both this application and the '345 patent the claims encompass detection of the same protein. Note that instant claims 2 - 5 do not require detection of multiple proteins of the heterocomplex; the methods are sufficiently broad that they encompass detecting one molecule of the complex when it is part of such a complex.

Conclusion

12. Claims 2 – 7 and 10 are rejected.

13. Claims 8 – 9 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL KOLKER whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E. Kolker, Ph.D./
Patent Examiner, Art Unit 1649
September 8, 2008